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ABSTRACT

of the dissertation for the degree of Doctor of Sciences

**CHARACTERISTICS, TREATMENT AND PREVENTION OF
GESTATIONAL AND PERINATAL COMPLICATIONS IN
OBESE PREGNANT WOMEN**

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GENERAL CHARACTERISTICS OF THE RESEARCH WORK

The relevance of the problem. Obesity is a serious medical, social, and economic problem in our modern society. Even though its consequences, including ischemic heart disease, arterial hypertension, type 2 diabetes mellitus, and gastrointestinal tract diseases have been given enough attention in theoretical and practical medicine, the problem of obesity has remained in the "shadow" for a long time as one of the most important causes of diseases with alimentary risk factors^{1,2}. WHO predicts that by 2025, the number of people diagnosed with obesity in the world will exceed 700 million, and by 2030, 2.2 billion people could be overweight and 1.1 billion could be obese³. Of particular concern is the significant increase in the number of women of reproductive age with overweight and obesity. In recent decades, maternal obesity has become one of the most important risk factors in obstetric practice⁴. Obesity is a global societal problem that affects the health of pregnant women, not only the mother but also the fetus. The prevalence of maternal obesity is mainly associated with social, educational, demographic, and ethnic factors⁵.

¹Xue, R. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirtyone prospective studies / R. Xue, Q. Li, Y. Geng, et al. // *Br J Nutr.*, – 2021, – № 12, – p. 1–11.

² Araújo, F.G. Prevalence trends of overweight, obesity, diabetes and hypertension among Brazilian women of reproductive age based on sociodemographic characteristics / F.G. Araújo, G. Velasquez-Melendez, M.S. Felesbino-Mendes // *Health Care Women Int.*, – 2019, – vol. 15.– p. 1-21.

³ World Health Organization. Obesity and overweight. Geneva: WHO; 2020. Accessed June 17, 2021. <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>.

⁴ Безрукова, Д. А. Ранние и поздние эффекты материнского ожирения в диаде "мать-дитя" / Д. А. Безрукова, А. А. Джумагазиев, Н. Ю. Отто // *Вопросы детской диетологии*, – 2021, – т. 19, -№ 4, – с. 46-55.

⁵ Goldstein, R.F. Gestational weight gain across continents and ethnicity: systematic review and meta-analysis of maternal and infant outcomes in more than one million women / R.F. Goldstein, S.K. Abell, S. Ranasinha [et al.] // *BMC Med.*, – 2018, – vol. 16, -№ 1, – p. 153.

Disturbance of fat metabolism during pregnancy causes several complications, the frequency of which is 42.5-85.0%⁶. This is primarily due to numerous complications of pregnancy associated with obesity, such as the risk of miscarriage (especially in the early stages), gestational diabetes, premature birth, premature abruption of a normally located placenta, abnormal contractility of the uterus, and delayed fetal development. On the contrary, the development of a large fetus may be complicated by postpartum hemorrhage. All this cannot but increase the risk of maternal and perinatal pathology and mortality⁷.

Epidemiological and experimental studies suggest that susceptibility to obesity may be programmed through epigenetic changes caused by maternal nutrition during fetal development⁸. All epigenetic changes in a pregnant woman's body can disrupt metabolic programming, leading to increased postnatal pathology in the fetus and complications in both pregnancy and the postpartum period for the mother. Pregnancy is a crucial stage in the formation of the "mother-placenta-fetus-newborn" system in obese women⁹.

The main role in the etiology and development of obesity is given to adipokines, which have local, systemic effects and play a complex role in the regulation of fat metabolism. Energy metabolism mediators, such as leptin, adiponectin, visfatin, resistin, etc., play an

⁶ Denison, F.C. Care of women with obesity in pregnancy: green-top guideline No72 / F.C. Denison, N.R. Aedla, O. Keag, [et al.] Royal College of Obstetricians and Gynaecologists // BJOG., – 2019, – vol. 126, - № 3, - e62-e106.

⁷ Pigatti, S.F. Role of Body Mass Index and gestational weight gain on preterm birth and adverse perinatal outcomes / S.F. Pigatti, R.T. Souza, J.G. Cecatti // Sci Rep., - 2019, - 9(1), -p.13093.

⁸ Сметанина, С.А. Ожирение у матери и метаболические нарушения у потомства: возможные влияния / С.А. Сметанина, Л.А. Суплотова, Е.Б. Храмова, Я.В. Гирш // Бюл. сибир. мед., - 2018,- Т. 17,- № 2,- с. 93-99.

⁹ Евсюкова, И. И. Молекулярные механизмы функционирования системы «Мать-плацента-плод» при ожирении и гестационном сахарном диабете / И. И. Евсюкова // Молекулярная медицина, – 2020, – т. 18, -№ 1, – с. 11-15.

important role in the homeostasis of adipose tissue^{10,11,12}. Adipokines not only have energy but also participate in the regulation of immunological processes that continuously occur in the body under the influence of internal and external environmental factors. The presence of chronic inflammation in obese women during pregnancy triggers a cascade of reactions that lead to the formation of an inflammatory environment in the mother's body¹³.

Today, the ideal is direct detection of patients with metabolic disorders at the stage of pregnancy planning, but the stages of pre-pregnancy preparation are not always possible^{14,15,16}. Therefore, the most optimal option in modern conditions is to improve the stages of monitoring of a patient with metabolic disorders immediately after the moment of direct control with the possibility of carrying out timely and effective preventive measures aimed at minimizing both obstetric and perinatal risks and complications. The most important task is to search for factors that will allow for predicting the risk of pregnancy complications in early gestation.

¹⁰ Дзугкоев, С.Г. Адипокины, ожирение и метаболические нарушения / С.Г. Дзугкоев, Ф.С. Дзугкоева, И.В. Можаяева, О.И. Маргиева // *Современные проблемы науки и образования*, -2020,- № 6, - с. 201.

¹¹ Andersson-Hall, U. Longitudinal changes in adipokines and free leptin index during and after pregnancy in women with obesity / U. Andersson-Hall, P. Svedin, H. Svensson [et al.] // *Int. J. Obes. (Lond).*, – 2020, – vol. 44 (3), – p. 675–683.

¹² Zieba, D.A. Roles of leptin and resistin in metabolism, reproduction and leptin resistance / Zieba D.A. // *Domestic animal endocrinology*, - 2020, -vol. 73, - p. 106-472.

¹³ Романцова, Т.И. Иммунометаболизм и метавоспаление при ожирении / Т.И. Романцова, Ю.П. Сыч // *Ожирение и метаболизм*, - 2019, - т. 16, -№ 4, - с. 3-17.

¹⁴ Радзинский, В.Е. Возможность оздоровления женщин с избыточной массой тела и ожирением на этапе прегравидарной подготовки / В.Е. Радзинский, А.В. Соловьева, В.М. Кулешов // *Акушерство и гинекология*, - 2023,- № 1,- с. 83-90.

¹⁵ Савельева, И. В. Особенности прегравидарной подготовки у женщин с ожирением / И. В. Савельева, С. В. Баринов, С. И. Блауман // *Вопросы гинекологии, акушерства и перинатологии*, – 2018, – т. 17, -№ 5, – с. 29-33.

¹⁶ Price, S. A Preconception management of women with obesity: A systematic review / S. A Price, P. Sumithran, A. Nankervis [et al.] // *Obes Rev.*, – 2019, – vol. 20, - № 4, – p. 510-526.

Thus, using a complex of clinical, medical and biological, social, laboratory studies and methods of mathematical and statistical prediction, the study of the influence of obesity and its metabolic complications on the course of pregnancy and childbirth will make it possible to clarify the pathogenetic mechanisms of obesity development in women and to prevent pregnancy complications on time.

Objective of the study. The dissertation presents the results of a retrospective and prospective cohort study among pregnant women by the provisions of the Declaration of Helsinki of the World Medical Association. All clinical studies were carried out based on the Department of Obstetrics and Gynecology II of the Azerbaijan Medical University. The retrospective study made it possible, based on the analysis of anamnesis and questionnaires, to present the clinical, anamnestic, and medical-social characteristics of 470 pregnant women. The material for the prospective study was a comprehensive clinical and laboratory examination of 120 pregnant women. The control group consisted of 80 practically healthy pregnant women with normal body weight.

Purpose of the study. To study the state of reproductive health in obese women, to clarify the role of obesity in the development of obstetric complications depending on the severity of changes in metabolic processes, and to determine the features of the relationship “mother-fetus” in obese pregnant women.

Research objectives:

1. Determine the prevalence of obesity among women of reproductive age.
2. Determine the pathogenetic factors contributing to the formation of gestational complications in obese women.
3. To determine the features of lipid, protein, and carbohydrate metabolism, cytokine status, hemostasis, clinical and hemodynamic parameters, and the amount of adipokines in overweight and obese pregnant women in the first, second, and third trimesters of pregnancy.

4. To study the role of risk factors in the formation of obesity and evaluate their relationship in pregnant women with overweight and obesity.
5. Based on the study of the uteroplacental and fetoplacental circulation, the state of the fetoplacental complex, and the parameters of the morphological study of the placenta, umbilical cord, and fetal membranes in obstetric pathologies associated with obesity.
6. To study the clinical course of pregnancy, childbirth, the postpartum period, and perinatal outcomes in pregnant women with overweight and obesity.
7. Determine the cause-and-effect relationship between obesity and obstetric complications and identify risk groups among pregnant women.
8. Assess the impact of preventive measures on newborns in patients with overweight and obesity, the course of pregnancy, the course of childbirth, and the consequences.
9. Identify risk groups for the development of perinatal pathology among children born to women with overweight and obesity.
10. Develop a set of therapeutic and preventive measures, starting from the pregravid level, to prevent complications in pregnant women with overweight and obesity and ensure high-quality delivery.

Research methods. A comprehensive general clinical, medical-social, anthropometric, instrumental, and clinical-laboratory examination was carried out. Clinical methods: medical history, general and gynecological examination. Laboratory methods: a study of carbohydrate metabolism (plasma glucose and immunoreactive insulin, HbA1c, oral glucose tolerance test, determination of insulin resistance using the HOMA-IR and CARO indices); study of lipid metabolism (TC, TG, LDL, HDL, VLDL, ALT, AST, ALP level, level of adiponectin, leptin, resistin, visfatin in blood serum); study of systemic inflammation markers (CRP, IL-6, TNF α). Morphological study of the placenta and the umbilical cord using morphometric and immunohistochemical methods. Instrumental research methods:

anthropometry (measurement of weight, height, WC, TC, WC/TC, BC), blood pressure measurement. Methods of statistical analysis (Shapiro-Wilk, Mann-Whitney, Kruskal-Wallis criteria, Pearson correlations, Cramer's criterion, determination of the clinical informativeness of diagnostic tests).

The main provisions for the defense:

1. Obese pregnant women are characterized by high anthropometric indices: BMI ($39.5 \pm 0.57 \text{ kg/m}^2$), WHtR (0.56 ± 0.003 units), WC/HC (0.90 ± 0.004 units), which corresponds to the abdominal type of distribution of adipose tissue and mainly the II degree of severity of obesity (44.6%), have eating disorders mainly in restrictive (19.2%) and mixed (51.6%) types with hyperphagic reaction to stress and low physical activity (91.1%).
2. In obese pregnant women, with increasing gestational age, physiological dyslipidemia is transformed into pathological dyslipidemia in the form of hypercholesterolemia, and hypertriglyceridemia, and the presence of close connections between the lipid profile and BMI parameters, there is an increase in the atherogenic potential of the blood, blood serum, as well as a dynamic deterioration in carbohydrate metabolism in the form of hyperglycemia on the background of increased insulin resistance.
3. The imbalance of adipokine status in obese women is determined by dysfunction of adipose tissue, manifested by hypoadiponectinemia, hypovisfatinemia, and hyperleptinemia, characterized by leptin resistance and an inflammatory state characterized by increased levels of systemic inflammation markers.
4. In obese pregnant women, the structural organization of the placenta, significant expression of the immunohistochemical marker CD3+, and progressive pathological changes indicate the presence of circulatory disorders in the chorionic villi with the possible formation of decompensatory placental insufficiency.

5. Obesity is associated with the development of moderate preeclampsia in the second half of pregnancy (RR=6.67; CI=2.10-21.10; $\chi^2=15.482$; Cramer's criterion=0.279; $p<0.001$), chronic fetal hypoxia (RR=8.00; CI = 1.06-60.32; $\chi^2 = 6.047$; Cramer's criterion = 0.174; $p = 0.014$) and fetal macrosomia (RR = 2.72; CI = 1.95-3.78; $\chi^2 = 20.535$; Cramer's criterion = 0.394; $p<0.001$) is a significant risk factor.
6. A pathogenetically based model for identifying and predicting the development of obesity and associated metabolic disorders in early pregnancy opens up the possibility of managing individual risk factors for obstetric complications.

The scientific novelty of the research:

- For the first time, a comprehensive study of the influence of obesity and its metabolic complications on the course of pregnancy and childbirth was carried out using adequate clinical, biomedical, social, and laboratory research methods in the dynamics of the gestational period.
- The state of metabolic homeostasis in obese pregnant women was studied and the correlation between metabolic parameters and clinical and anthropometric data was determined.
- Serum levels of adiponectin, leptin, visfatin, and resistin in obese pregnant women were compared with the levels of these adipokines in normal-weight pregnant women. A correlation has been established between adipokine status indicators and anthropometric indicators and metabolic disorders associated with obesity.
- The prognostic significance of clinical and metabolic disorders during pregnancy has been determined, and the most important risk factors for the development of metabolic complications in obese pregnant women have been identified - genetic load, nutritional disorders, and low physical activity.
- The association of hormonal-metabolic parameters in pregnant women in the first trimester showed a close relationship between the level of adipocytokines, markers of systemic inflammation, insulin resistance, dyslipidemia, and anthropometric data.

- Morphological and immunohistochemical changes were determined in the placenta of women with normal body weight, obesity, and metabolic disorders.
- Based on the calculation of relative risk indicators, 95% confidence intervals, and analysis of combined tables, the decisive role of obesity and concomitant metabolic disorders in the development of obstetric complications and negative perinatal outcomes has been proven.
- A model has been developed for predicting the development of metabolic disorders in early pregnancy based on methods of mathematical and statistical analysis of clinical and anamnestic predictors, biochemical parameters of metabolism, changes in systemic markers of inflammation, and assessment of adipocytokine status.

Practical significance of scientific work.

- Based on comprehensive clinical and laboratory studies, the course of pregnancy in women with obesity and metabolic disorders, risk factors and their role in the development of obstetric and pregnancy complications, as well as new knowledge were obtained.
- For practical medicine, information is provided on the characteristics of the metabolic profile at different stages of gestation.
- An individual risk assessment of the obtained clinical and laboratory associations is recommended, taking into account the prevention of pregnancy complications.
- Based on the results of the study, the basic principles of a two-stage program of measures when planning pregnancy in obese women have been proposed.

Application of research results in practice.

Practical recommendations, and algorithms for pregnancy and childbirth, proposed in scientific work, are used in practical activities of the Department of Obstetrics and Gynecology of the Educational-Surgical Clinic of AMU. The dissertation materials are used in the

educational process of the II Department of Obstetrics and Gynecology of the AMU.

Approbation of the dissertation materials.

Dissertation materials were presented at the VII International Scientific Conference in Brussels (“Diagnosis of Causes of obesity in pregnant patients”, General question of world science. Collection of scientific papers on materials VII International Scientific Conference, Brussel, 2019), at the VIII International Scientific Conference in Amsterdam («On the issue of the risk of pregnancy complications», General question of world science. Collection of scientific papers on materials VIII International Scientific Conference, Amsterdam, 2019), at the International Congress on Global and Regional Development in Baku (“Pathomorphological characteristics of the umbilical cord in obese pregnant women”, International Congress on Global and Regional Development, Baku, December 19-21, 2023), and at the II International Congress of Turkish and World Women's Studies in Baku (“Course of delivery and postpartum period in pregnant women with obesity and metabolic disorders”, 2nd International Turkish and World Woman’s Studies Congress, Baku, January 27-30, 2024).

A preliminary discussion of the dissertation work took place on June 10, 2023, at an interdepartmental meeting (meeting No. 02), and a discussion of the scientific seminar took place on December 20, 2023, at the scientific seminar of the Dissertation Council ED 2.06 (protocol No. 02) at AMU.

The organization in which the dissertation work was carried out. The dissertation work was carried out at the Department of Obstetrics and Gynecology II of the Azerbaijan Medical University.

Published works. 22 scientific works have been published on the topic of the dissertation. Of these, 16 articles and 8 theses.

Structure and volume of the dissertation. The dissertation was annotated on 340 pages (402812 characters) printed on a computer and consists of “Introduction”, 8 chapters, “Conclusions”, “Results” and “Practical recommendations”: Introduction (volume: 18608 characters), Chapter I. “Literature review” (volume: 116355 characters), Chapter II. “Materials and methods” (volume: 17927

characters), Chapter III. "Clinical and anamnestic characteristics of examined pregnant women" (volume: 43749 characters), Chapter IV. "The state of metabolic hemostasis in pregnant women in the dynamics of prospective observation" (volume: 28310 characters), Chapter V. "Adipokines, metabolic markers and markers of systemic inflammation in pregnant women" (volume: 38156 characters), Chapter VI. "Macroscopic and pathomorphological characteristics of changes in the placenta and umbilical cord in pregnant women with gestational and perinatal complications during pregnancy" (volume: 25287 characters), Chapter VII. "Prognostic significance of clinical and metabolic disorders during pregnancy" (volume: 26886 characters), Chapter VIII. "The course of pregnancy, childbirth and the condition of newborns in mothers with obesity" (volume: 17469 characters), "Conclusion" (volume: 62706 characters), "Results" (volume: 6311 characters), "Practical recommendations". (volume: 1048 characters). The dissertation is illustrated with 79 tables, 16 diagrams, 13 graphics and 33 figures. The bibliography includes 325 sources, of which 13 are in Azerbaijani, 183 in Russian, and 129 in English.

MAIN CONTENT OF RESEARCH WORK

Materials and methods of research. The retrospective study made it possible, based on the analysis of anamnesis and questionnaires, to present the clinical, anamnestic, and medical-social characteristics of 470 pregnant women. The retrospective study was based on an analysis of the dates of birth of 125 women with abdominal obesity, 218 pregnant women with arterial hypertension, 88 pregnant women with arterial hypertension and obesity, and 39 pregnant women with hyperglycemia. The material for the prospective study was a comprehensive clinical and laboratory examination of 120 pregnant women (59 with arterial hypertension, 29 with obesity, 23 with arterial hypertension and obesity, 9 with diabetes mellitus type 2). The control group consisted of 80 practically healthy pregnant women with normal body weight (BMI before pregnancy <25). This group included pregnant women without a history of chronic somatic

diseases and obstetric and gynecological complications in the phase of exacerbation and decompensation. Blood pressure, carbohydrate, and lipid metabolism parameters were within the reference parameters.

Complex general clinical, medical-social, anthropometric, instrumental, and clinical-laboratory studies were carried out according to the objectives. All clinical studies were conducted based on the Department of Obstetrics and Gynecology II of Azerbaijan Medical University. Observation and examination of pregnant women included anamnesis collection, general physical examination of respiratory, circulatory, digestive, urinary systems and mammary glands, anthropometry (calculation of height, weight, waist circumference (WC), hip circumference (HC), body mass index (BMI), gynecological examinations.

Inclusion criteria:

- women aged 18 to 45 years with a singleton pregnancy that occurred in the natural cycle and ended in term labor, consent to participate in the study;
- abdominal obesity (WC >80 cm, WC/HC >0.85) was the main criterion;
- additional criteria: elevated levels of triglycerides and LDL; high blood pressure; elevated fasting plasma glucose levels.

Exclusion criteria:

- multiple pregnancies, pregnancies resulting from assisted reproductive technologies, refusal to participate in the study;
- pregnant women who did not meet the listed inclusion criteria.

To solve the tasks set, general clinical examination methods were used, taking into account the influence of hereditary and medico-social risk factors. General clinical examination includes anamnesis collection and general and gynecological examination. Complaints, peculiarities of personal and family history, information about the presence of somatic and gynecological pathology, and the results of an objective examination were analyzed. All information was entered into questionnaires with the identification of risk factors for the development of pathology. Eating behavior and physical activity levels were assessed in all patients.

From the moment of reaching reproductive age, the following parameters were identified:

- socio-biological factors: age, place of residence, place of work, occupational hazards, bad habits, psycho-emotional stress, marital status, housing conditions;
- obstetric and gynecological anamnesis: menstrual function, sexual function, reproductive function, gynecological history;
- extragenital diseases
- objective status: height, constitutional type, BMI, WC/HC index.

Laboratory methods of research include the determination of several parameters of carbohydrate and fat metabolism in blood. To study carbohydrate metabolism, fasting venous blood glucose concentration, immunoreactive insulin, and glycated (glycosylated) hemoglobin (HbA1c) were measured. After glucose determination, an oral glucose tolerance test was performed. A small homeostasis model (Homeostasis Model Assessment-HOMA) was used to assess the degree of insulin resistance by determining the HOMA-IR index. Another parameter of insulin resistance is the calculation of the CARO coefficient according to the formula.

The state of lipid metabolism was assessed by a lipidogram. The concentration of total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) was determined. The study was performed three times during pregnancy, at 8-12, 18-20 and 34-36 weeks of gestation.

Microalbuminuria in pregnant women was determined by turbidimetric method in the morning urine.

The concentration of leptin, adiponectin, resistin and visfatin in the studied serum was determined by enzyme-linked immunosorbent assay (ELISA).

The study of the level of markers of systemic inflammation includes determination of the concentration of C-reactive protein (CRP) and interleukin-6, tumor necrosis factor- α (TNF- α). Solid-phase sandwich enzyme-linked immunoenzyme method (ELISA) was

used to determine the concentration of IL-6 and TNF- α in blood plasma.

The pathomorphologic study included placentas, umbilical cords and placental membranes obtained from 35 pregnant women. The study was conducted at the Bureau of Pathological Anatomy of the "Forensic Medical Examination and Pathological Anatomy" Association of the Ministry of Health of the Republic of Azerbaijan, at the Department of Pathological Anatomy of Azerbaijan Medical University, and at the Educational-Surgical Clinic of the Azerbaijan Medical University.

Blood pressure was measured by a noninvasive auscultatory method using an arrow manometer according to the standard method of N.S. Korotkov in a sitting position in a comfortable posture, with the arm on the table at the level of the heart, the lower edge of the standard cuff (width 12-13 cm, length 35 cm) 2 cm above the elbow folder. Measurements were taken at rest (after 5 minutes of rest) 2 times with an interval of at least a minute - if the difference was equal to or more than 5 mm Hg, one additional measurement was taken and the average values were calculated. Blood pressure was measured in both arms, if it was different, the higher values were used. The values were recorded to an accuracy of 2 mmHg.

To diagnose abdominal obesity, anthropometric measurements were performed on all subjects. The anthropometric examination included the determination of body weight, height, WC, BMI, and WC/HC ratio. Body weight was determined using medical scales with an accuracy of 0.1 kg. Height was measured with a wall-mounted height meter. Waist circumference was measured with a centimeter tape in a standing position, in the phase of exhalation, resting on both feet, arms lowered along the torso. The measurement was taken at the middle of the distance from the lower edge of the rib arch to the crest of the iliac bone. Hip circumference was measured using a centimeter tape, measuring the circumference at the most protruding points at the level of the pubic symphysis in front and the greater trochanter of the femur on the side.

The WC/TC ratio was calculated, which was used to indirectly judge the type of adipose tissue distribution. A value of WC/TC >0.85 confirmed the presence of excess adipose tissue in the abdominal region.

Statistical data analysis was performed using the MedCalc statistical software package for biomedical research. The results obtained were assessed by methods of statistical description and testing of statistical hypotheses. The compliance of quantitative characteristics in the formed groups with the law of normal distribution was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk criteria. A comparison of central parameters in the study groups was carried out using nonparametric Mann-Whitney tests and the Kruskal-Wallis test.

Numerical data are presented as means \pm error of the mean ($M \pm m$). The strength and relationship between phenomena or signs were assessed using the Pearson pair correlation coefficient (r).

When assessing the differences in qualitative characteristics in independent samples, the method of determining absolute and relative frequencies and conjugation tables using the χ^2 criterion was used. In addition to assessments of the Pearson χ^2 criterion and the achieved level of statistical significance of this criterion, we evaluated the intensity of association of the analyzed qualitative characteristics using the V-Kramer coefficient.

To assess the independent contribution of factors to the probability of an event occurring, the calculation of the odds ratio (OR) for each of the statistically significant factors and its 95% confidence interval (95% CI) was used. Using the decision matrix principle, the performance of diagnostic tests was assessed. The characteristics of diagnostic tests were determined according to the four-field table. The critical value of the level of statistical significance (p) in testing the null hypotheses was assumed to be 0.05.

CLINICAL - ANAMNESTIC CHARACTERISTICS OF PREGNANT WOMEN

The present study allowed us to present the clinical-anamnestic and medical-social characteristics of 550 pregnant women based on the analysis of birth histories and the conducted survey. Among the examined patients, 213 (45.3%) pregnant women were diagnosed with obesity (group 1), 218 (46.4%) with arterial hypertension (group 2), and 39 (8.3%) with hyperglycemia (group 3). The control group included 80 pregnant women with no concomitant pathology. At the time of dispensary registration, all women with a gestational age of up to 10 weeks underwent a standard anthropometric examination with measurement of body weight (in kg) and height (in cm). Waist circumference (WB) and thigh circumference (TC) were measured during anthropometric examination.

According to our study, the majority of obese women (48.8%) were aged from 20 to 29 years (under 20 years - 2.8%, 20-29 years - 48.8%, 30-34 years - 29, 1%, 35-39 years old - 15.5%, 40 years and older - 3.7%) (Figure 1). The average age of women included in the main group was 29.8 ± 0.54 years [95% CI 29.73-25.87], and in the control group - 25.7 ± 0.47 years [95% CI 25.60 -25.80].

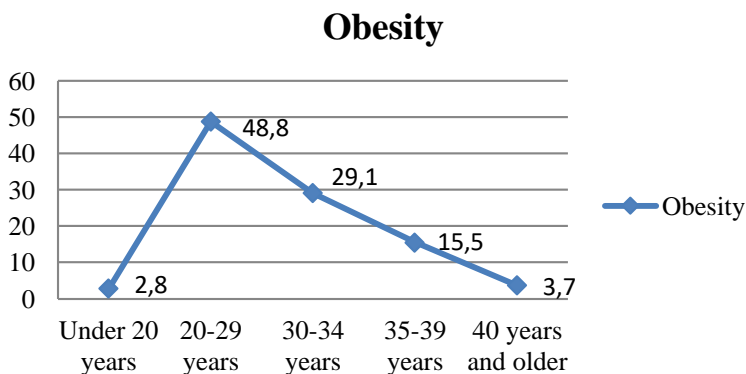


Figure 1. Obesity in pregnant women of different ages

Among the women we examined, the majority of those who took part in our survey (n=114; 53.5%) noted that their body weight began to increase during puberty. The majority of women who participated in the survey (n=129; 60.6%) mention increased appetite as the main factor causing weight gain. Other patients point to prolonged psycho-emotional stress, childbirth and raising children, lack of physical activity, etc. as provoking factors. Analysis of hereditary factors for obesity shows that 84.0±2.51% (n=179) (p<0.05) of obese pregnant women have 1st-degree relatives in the family who are overweight and obese.

Based on the results obtained, the central obesity indices were calculated, which allows us to objectively assess the degree of its severity. The easiest and most accessible way to diagnose obesity is to determine BMI. This, along with other anthropometric measurements, is used as a key marker for the diagnosis of obesity during pregnancy. The mean BMI in obese pregnant women was 39.5±0.57 kg/m², which was 1.6 times higher than in women in the control group (24.1±0.34 kg/m², p<0.001).

When comparing anthropometric parameters in pregnant women with obesity, it was found that the values of the WC/TC index were higher, which corresponds to the abdominal type of distribution of adipose tissue. In obese pregnant women, the WC/TC ratio corresponds to 0.90±0.004 units, which honestly exceeds the value of the same indicator in women in the control group (0.83±0.004 units, p<0.001). Of the observed pregnant women with abdominal obesity, 43 (20.2%) had degree I obesity, 95 (44.6%) degree II, and 75 (35.2%) degree III.

Pregnant women suffering from obesity have applied various complaints, which are related to excess body weight and the development of accompanying pathological processes in the body. The structure of complaints was dominated by complaints of overweight (100% of patients), sleep disorders, headaches, back and joint pain.

The structure of complaints of pregnant women depending on the severity of obesity was analyzed. The complaints presented are

different, but women mainly complained of pain syndromes (headaches, back pain, and joint pain) and psycho-emotional disorders.

Of the total number of obese pregnant women, 155 (72.7%) of them complained of unilateral or symmetrical headaches of varying intensity. The provoking factors for headaches were usually forced position of the head and neck and physical and mental stress. Often headaches were noted immediately after morning awakening.

Pregnant women in the main group also had pain of varying intensity in the neck, back, and lumbar region, pain in the joints of the extremities, mainly the lower extremities. Back pain was detected in 172 (80.7%) women. 155 (72.7%) obese pregnant women complained of joint pain.

The analysis of the presented complaints allows us to consider that their severity has a direct correlation with the degree of obesity. As the severity of obesity increased, the number of women presenting complaints also increased. It should be noted that the number of women presenting various complaints increased significantly when comparing the group of patients with obesity I degree with similar manifestations in patients with obesity II and III degrees (O_{I-II} and O_{I-III}). There were no quantitative differences in the severity of complaints of joint pain and sleep disturbance in the group of women with obesity II and III degrees ($p > 0.05$).

Assessment of eating behavior in obese patients includes monitoring of food intake. It was found that almost half ($47.89 \pm 3.42\%$) of the obese women had irrational and excessive eating behavior ($3.75 \pm 2.12\%$ in the control group, $p < 0.001$), and 12.8% of the patients abused various tonic drinks ($p < 0.05$). The majority of women who participated in the survey consumed high-calorie carbohydrate food (sweets, candy) due to constant uncontrollable hunger between the main meals.

The nature of food intake during the day was subjected to special assessment. The maximum amount of food was consumed for dinner in the majority of examined pregnant women. Evening and/or nocturnal hyperphagia (eating more than 25% of daily caloric intake

after dinner or at night 2 or more times a week) was found in 113 (53.05±3.42%) pregnant women with obesity and in 12 (15.0±3.99%) patients of the control group ($p<0.001$).

Combining meals and other activities (reading, working, watching TV) were noted with equal frequency in both groups ($p>0.05$).

As a result of the study, it was revealed that in the structure of eating behavior disorders, the leading place is occupied by restrictive and mixed types (19.2% and 51.6%, respectively). Moreover, the mixed type of eating behavior was dominated by the emotigenic component. When assessing the dependence of eating behavior on the degree of obesity, no significant differences in the representation of one or another form of disorder were found.

The level of education is one of the known significant factors of obesity and affects the prevalence of obesity. The studies revealed that in the group with obesity, 58.4% of women ($n=73$) had secondary education, 3.2% ($n=4$) had specialized secondary education, 15.2% ($n=19$) had incomplete higher education, 20.8% ($n=26$) had higher education, and 2.4% ($n=3$) had primary education.

Among pregnant women with higher and incomplete higher education, the proportion of obese women was statistically significantly lower compared to women with secondary and specialized secondary education (36.0% and 61.6%, respectively, $p<0.05$). In the control group, 52.5% ($n=42$) had secondary education, 3.8% ($n=3$) had incomplete higher education, 28.8% ($n=23$) had higher education, and 15.0% ($n=12$) had primary education.

According to their professional affiliation, the observed women in the main group were distributed as follows: students - 1 (0.47±0.43%), employees - 34 (15.96±2.51%), housewives - 178 (83.57±2.54%). In the control group: students - 4 (5.0±2.44%), employees - 16 (20.0±4.47%), workers - 1 (1.25±1.24%), housewives - 59 (73.75±4.92%) ($p>0.05$).

Marital status in our study was not reflected in the incidence of obesity. According to the results of questionnaire data, it was found that 85.45±2.42% of women were officially married and 14.55±2.42%

of women were unmarried or divorced. In the control group, $78.75 \pm 4.57\%$ of women were officially married and $21.25 \pm 4.57\%$ of women were outside marriage ($p > 0.05$).

The social structure of the observed patients was heterogeneous. In particular, when determining the place of residence, it was found that 141 ($66.2 \pm 3.24\%$) women lived in urban areas and 72 ($33.8 \pm 3.24\%$) obese patients lived in rural areas ($p < 0.001$). Among women in the control group, 74 ($93.75 \pm 2.71\%$) lived in the city and 6 ($7.5 \pm 2.94\%$) lived in rural areas ($p < 0.001$).

The study of the social and domestic status of the examined pregnant women showed that at the time of the study, $35.21 \pm 3.27\%$ of the patients reported material difficulties (36.25% in the control group). $49.77 \pm 3.43\%$ of women ($48.75 \pm 5.59\%$ in the control group) assessed their financial situation as average, and $15.02 \pm 2.45\%$ of women (15.0% in the control group) assessed it as good.

However, our analysis did not demonstrate an association of low and middle-income with the incidence of obesity.

It is known that one of the most significant, but at the same time modifiable risk factors is smoking. Assessing the patients' addiction to bad habits, it was found that 1.6% of women smoked before pregnancy, and 6.4% of obese patients consumed alcoholic beverages in insignificant amounts.

The results of the study show that $91.08 \pm 1.95\%$ of women in the main group have low or no physical activity, while in the control group, this fact is observed in $10.0 \pm 3.35\%$ of women ($p < 0.001$). Eating disorders of the emotional type were identified in 23 (10.8%) of the examined pregnant women. The external type of eating behavior was diagnosed in 30 (14.1%) women. Restrictive eating behavior was identified in 41 (19.2%) women. When assessing the structure of eating behavior, mixed eating disorders were identified in 110 (51.6%) women.

Concomitant extragenital pathology can have a significant impact on the formation of women's reproductive function and all parameters of homeostasis, which ensures the functioning of this system. All examined obese women had extragenital diseases.

The analysis of the nature and frequency of comorbidities shows that in all patients of the main group (100.0%) the main component of the metabolic syndrome is obesity. In the main group of patients, there were more diseases of the cardiovascular system ($40,38 \pm 3,36$ %, in the control group - $12,5 \pm 3,7$ %, $p < 0,001$), diseases of gastrointestinal tract ($30,52 \pm 3,16$ %, in the control group - $16,25 \pm 4,12$ %), thyroid diseases ($28,17 \pm 3,08$ %, in the control group - $10,0 \pm 3,35$ %, $p < 0,05$), ARVI and influenza ($27,25 \pm 3,0$ %, in the control group - $20,0 \pm 4,47$ %, $p > 0,05$).

In an analysis of the delivery history, 218 out of 550 pregnant women were found to have arterial hypertension with an incidence of 39.6% (218 out of 550). The age range of the patients was 18 to 46 years. The duration of arterial hypertension in the studied women ranged from 1 to 4 years, with an average of 1.7 ± 0.17 years.

Statistically significant differences were found between the groups in terms of systolic ($p < 0.001$), diastolic ($p < 0.001$), pulse ($p < 0.001$), and mean ($p < 0.001$) arterial pressure levels during the initial examination. In women of the control group with normal body weight, systolic (100.8 ± 0.87 mm Hg), diastolic (64.4 ± 0.71 mm Hg), pulse (36.4 ± 0.15 mm c. milk.) and average (76.1 ± 1.22 mm c. milk) minimum value of arterial pressure was recorded. Based on anamnestic data, it was found that 95.9% of respondents with arterial hypertension ($n=209$) had high arterial pressure, which indicates the high awareness of patients. In addition, only 11.9% of patients ($n=26$) had previously consulted a doctor and received an appropriate clinical diagnosis.

The obese pregnant women we observed in 30.5% of cases suffered from gastrointestinal diseases: chronic cholecystitis, pancreatitis, and biliary stone disease. Symptoms of these diseases are heartburn, nausea, abdominal pain, belching, and others, which motivates patients to consume non-coarse, easily digestible high-calorie foods.

28.1% of women previously or at the time of the study had various types of disorders of the thyroid system (autoimmune

thyroiditis, hypothyroidism, thyrotoxicosis, structural changes in the thyroid gland).

At the same time, it should be noted that when recruiting pregnant women into the study, it was practically impossible to select healthy women without anamnestic indications of various diseases. Therefore, of all the women recruited in the control group, 12.5% had a history of cardiovascular diseases, 16.2% were diagnosed with diseases of the digestive system, 10.0% with thyroid diseases, and 20.0% with respiratory viral pathology.

Thus, as a result of the study, it was established that obese pregnant women had the following medical and social characteristics. The average age of obese pregnant women was 29.8 ± 0.54 years, among them, patients aged 20-29 years predominated (48.8%). In the vast majority of women, we examined (53.5%), body weight began to increase during puberty.

A hereditary predisposition to obesity was noted in 84.0% of pregnant women. In obese pregnant women, the WC/TC ratio was 0.90 ± 0.004 units, which is a sign of abdominal obesity. In pregnant women with abdominal obesity, 43 (20.2%) patients had an I degree of obesity, 95 (44.6%) had an II degree, and 75 (35.2%) had a III degree of obesity.

Obese pregnant women have various lifestyle disorders: irrational nutrition, insufficient outdoor activities, and low motor activity. The questionnaire survey revealed increased appetite in all women, which was accompanied by an increase in the volume and calories of food consumed with excessive fat and carbohydrates. Eating behavior disorder of the emotiogenic type was found in 10.8%, external type - in 14.1%, restrictive type - in 19.2%, and mixed type - in 51.6% of pregnant women. Normal eating behavior was observed in 4.3% of women.

At the time of registration, pregnant women with arterial hypertension had an average body weight of 79.5 ± 0.94 kg, a minimum weight of 51 kg and a maximum weight of 114 kg, the average body weight of women in the control group was 62.1 ± 0.87 kg, their minimum and maximum weight were 46 kg and 82 kg, respectively

($p < 0.001$). WC values ranged from 67 to 100 cm (82.8 ± 0.51 cm) in pregnant women with arterial hypertension and from 67 to 84 cm (73.4 ± 0.48 cm) in women with normal body weight in the control group ($p < 0.001$). EC values in pregnant women with arterial hypertension range from 78-107 cm (93.3 ± 0.40 cm), and in women with normal body weight in the control group - from 76-103 cm (88.1 ± 0.65 cm) ($p < 0.001$). In pregnant women with arterial hypertension, the average value of the WC/HR index was 0.89 ± 0.003 units, which significantly exceeds the same figure for women in the control group (0.83 ± 0.004 units, $p < 0.001$). The average WHtR value in pregnant women with arterial hypertension was 0.51 ± 0.001 units, which is honestly higher than the same indicator in women in the control group (0.46 ± 0.008 units, $p < 0.001$).

When risk factors were analyzed, the examined pregnant women were significantly more likely to have aggravated heredity for arterial hypertension ($n=193$; $88.53 \pm 2.16\%$) ($p < 0.05$). According to the results obtained, the odds ratio of developing arterial hypertension in pregnant women with hereditary predisposition was $OR=48.42 \pm 0.38$ (95% CI: 22.63-103.61), the chance of finding a risk factor was 7.72 (0.15 in the control group). The relative risk score was $RR=3.55 \pm 0.17$ (95% CI: 2.53-4.98); absolute risk was $EER=0.94$; relative risk reduction was $RRR=2.55$; risk difference was $RD= 0.68$.

Another risk factor for the development of arterial hypertension is obesity. At the same time, of the surveyed pregnant women, only 9 of them (4.1%) showed concern about excess body weight, 8 (3.7%) noted that excess body weight was disturbing them, 6 (2.8%) women tried to normalize body weight, of which only 1 (0.5%) achieved the result. Among the reasons for the development of obesity during a questionnaire survey, 1 (0.5%) woman indicated a hereditary predisposition, 1 (0.5%) - previous diseases, 7 (3.2%) - excess nutrition, 6 (2.8%) - low physical activity.

Smoking as a risk factor for the development of arterial hypertension was indicated by 3 (1.4%) women, alcohol consumption in small amounts before pregnancy - 16 (7.3%) patients.

Analysis of the nature and frequency of comorbidities showed that all pregnant women in this group (100.0%) had arterial hypertension ($p<0.001$). They were also diagnosed with cardiovascular diseases (excluding arterial hypertension) in $23.39\pm 2.87\%$, digestive diseases in $11.0\pm 2.12\%$, thyroid diseases in $25.69\pm 2.96\%$, kidney and urinary system diseases in $19.72\pm 2.7\%$, acute respiratory viral infections, and influenza in $48.17\pm 3.38\%$ of the examined subjects.

Thus, as a result of the study, it was found that arterial hypertension is currently one of the most common forms of pathology in pregnant women. Pregnant women with arterial hypertension had the following medical and social characteristics. The mean age of pregnant women with arterial hypertension was 27.8 ± 0.40 years. Analysis of office blood pressure data showed that in patients with arterial hypertension, systolic, diastolic, pulse and average blood pressure were 1.4-1.6 times higher than control values. When risk factors were analyzed, the examined pregnant women had a significantly higher incidence of aggravated heredity for arterial hypertension ($88.53\pm 2.16\%$).

Because obesity is a significant risk factor for the development of arterial hypertension, we evaluated the premorbid background in 88 pregnant women with arterial hypertension combined with obesity.

The analysis of birth dates revealed that the medical and social indicators of 218 pregnant women with arterial hypertension and 88 obese women with obesity on a background of arterial hypertension were significantly different from each other and the control group. The mean age of pregnant women with arterial hypertension and obesity was 30.5 ± 0.64 years [95% CI 30.37-30.63], which was higher than control and comparison groups ($p<0.05$).

All examined women had their blood pressure measured. When assessing office blood pressure at the time of the initial examination, statistically significant differences were established between the groups in the level of systolic ($p<0.001$), diastolic ($p<0.001$), pulse ($p<0.001$) and mean ($p<0.001$) blood pressure. The minimum value of systolic (100.8 ± 0.87 mmHg), diastolic (64.4 ± 0.71 mmHg), pulse

(36.4 ± 0.15 mmHg) and average (76.1 ± 1.22 mmHg) blood pressure was recorded in women in the control group with normal body weight.

In pregnant women with arterial hypertension and obesity, the average body weight at registration was 105.5 ± 1.64 kg, the minimum weight was 75 kg, the maximum was 153 kg. In women in the control group, the average body weight was 62.1 ± 0.87 kg, and the minimum and maximum were 46 kg and 82 kg, respectively ($p < 0.001$). WC values in pregnant women with arterial hypertension and obesity ranged from 72 to 101 cm (90.5 ± 0.78 cm), and with normal body weight in women in the control group - from 67 to 84 cm (73.4 ± 0.48 cm) ($p < 0.001$). TC values in pregnant women with arterial hypertension and obesity ranged from 84 to 113 cm (99.3 ± 0.74 cm), and with normal body weight in women in the control group - from 76 to 103 cm (88.1 ± 0.65 cm) ($p < 0.001$). The average BMI value in pregnant women with arterial hypertension and obesity was 40.8 ± 0.70 kg/m², which was 1.7 times higher than this indicator in women in the control group (24.1 ± 0.34 kg/m², $p < 0.001$). The average value of the WC/TC index in pregnant women with arterial hypertension and obesity corresponded to 0.91 ± 0.004 units, which significantly exceeded the value of this indicator in women in the control group (0.83 ± 0.004 units, $p < 0.001$). The average value of the WHtR index in pregnant women with arterial hypertension and obesity corresponded to 0.56 ± 0.002 units, which significantly exceeded the value of this indicator in women in the control group (0.46 ± 0.008 units, $p < 0.001$).

When risk factors were analyzed, pregnant women with arterial hypertension and obesity were significantly more likely to have an aggravated heredity for arterial hypertension ($n=67$; $76.14 \pm 4.54\%$) ($p < 0.001$). According to the results obtained, the odds ratio of developing arterial hypertension in pregnant women with hereditary predisposition was $OR=20.0 \pm 0.41$ (95% CI: 8.96-44.68), the chance of finding a risk factor was 3.19 (in the control group, 0.15). The relative risk score was $RR=3.68 \pm 0.19$ (95% CI: 2.50-5.41); absolute risk, $EER=0.85$; decreasing relative risk, $RRR=2.68$; risk difference, $RD=0.62$. Heredity for obesity was found in 68 ($77.27 \pm 4.47\%$) pregnant women with arterial hypertension and obesity. According to

the results obtained, the odds ratio of developing arterial hypertension in pregnant women with hereditary predisposition was $OR=13.6\pm 0.37$ (95% CI: 6.48-28.52), the chance of finding a risk factor was 3.4 (0.25 in the control group). The relative risk score was $RR=3.4\pm 0.2$ (95% CI: 2.28-5.05); absolute risk was $EER=0.81$; relative risk reduction was $RRR=2.4$; risk difference was $RD= 0.57$.

All pregnant women in this group (100.0%) had arterial hypertension and obesity ($p<0.001$). They were also diagnosed with cardiovascular diseases (excluding arterial hypertension) in $28.41\pm 4.81\%$, digestive diseases in $10.23\pm 3.23\%$ ($p<0.05$), thyroid diseases in $36.36\pm 5.13\%$ ($p<0.001$), kidney and urinary system diseases in $15.91\pm 3.9\%$, acute respiratory viral infections, and influenza in $18.18\pm 4.11\%$ of the examined subjects.

Thus, the association of arterial hypertension with obesity may indicate the role of metabolic shifts in the development of arterial hypertension in pregnant women. The medical and social parameters of the examined pregnant women with arterial hypertension and obesity differed significantly from the control group. Patients in the observation groups had a pre-morbid background in comparison with women in the control group.

When analyzing the birth histories of 550 pregnant women, hyperglycemia was detected in 39 of them, with a frequency of 7.1% (39 cases out of 550). The age range of the patients was from 18 to 46 years.

In pregnant women with hyperglycemia, the average body weight at registration was 84.7 ± 3.11 kg, the minimum weight was 54, the maximum was 138 kg. In women in the control group, the average body weight was 62.1 ± 0.87 kg, and the minimum and maximum were 46 kg and 82 kg, respectively ($p<0.001$). WC values in pregnant women with hyperglycemia ranged from 69 to 101 cm (85.7 ± 1.52 cm), and with normal body weight in women in the control group - from 67 to 84 cm (73.4 ± 0.48 cm) ($p <0.001$). TC values in pregnant women with hyperglycemia ranged from 81 to 115 cm (96.7 ± 1.47 cm), and with normal body weight in women in the control group - from 76 to 103 cm (88.1 ± 0.65 cm) ($p <0.001$). The average BMI

value in pregnant women with hyperglycemia was $33.0 \pm 1.20 \text{ kg/m}^2$, which was 1.4 times higher than this indicator in women in the control group ($24.1 \pm 0.34 \text{ kg/m}^2$, $p < 0.001$). The average value of the WC/TC index in pregnant women with hyperglycemia corresponded to 0.89 ± 0.008 units, which significantly exceeded the value of this indicator in women in the control group (0.83 ± 0.004 units, $p < 0.001$). The average value of the WHtR index in pregnant women with hyperglycemia corresponded to 0.53 ± 0.002 units, which significantly exceeded the value of this indicator in women in the control group (0.46 ± 0.008 units, $p < 0.001$).

When analyzing risk factors in pregnant women with hyperglycemia, there was a family history of diabetes mellitus ($n=25$; $64.1 \pm 7.68\%$) ($p < 0.01$), obesity ($n=10$; $25.64 \pm 6.99\%$) ($p > 0.05$) and arterial hypertension ($n=5$; $12.82 \pm 5.35\%$) ($p > 0.05$).

According to the results obtained, the odds ratio for developing diabetes mellitus in pregnant women with hyperglycemia was $OR=33.92 \pm 0.61$ (95% CI: 10.22-112.6), the chance of finding a risk factor was 1.78 (in the control group - 0.05). The relative risk was $RR=5.54 \pm 0.25$ (95% CI: 3.35-9.16); absolute risk - $EER=0.86$; relative risk reduction - $RRR=4.54$; risk difference - $RD= 0.70$.

Analysis of the nature and frequency of comorbidities showed that 32 pregnant women in this group ($82.05 \pm 6.15\%$) had previously been diagnosed with type 1 diabetes mellitus ($p < 0.001$), 4 ($10.26 \pm 4.86\%$) with type 2 diabetes mellitus ($p < 0.01$), and 3 ($7.69 \pm 4.27\%$) with gestational diabetes mellitus ($p < 0.05$). They were also diagnosed with obesity in 13 ($33.33 \pm 7.55\%$) ($p < 0.001$), digestive diseases in $12.82 \pm 5.35\%$, thyroid diseases in $7.69 \pm 4.27\%$, kidney and urinary system diseases in $7.69 \pm 4.27\%$, acute respiratory viral infections, and influenza in $28.21 \pm 7.21\%$ of the examined persons ($p > 0.05$).

Thus, when analyzing anamnestic data in pregnant women with impaired carbohydrate metabolism, a retrospective study revealed that in this group, pregnant women aged 20-29 years (51.3%), with $BMI 33.0 \pm 1.20 \text{ kg/m}^2$ ($p < 0.001$) were significantly more common.

Aggravated heredity for diabetes mellitus was statistically significant ($64.1 \pm 7.68\%$) ($p < 0.01$).

METABOLIC HAEMOSTASIS IN PREGNANT WOMEN IN THE DYNAMICS OF PROSPECTIVE OBSERVATION

To identify the characteristics of lipid metabolism, we conducted a detailed analysis of lipid spectrum indicators in women included in the main and control groups. For this purpose, in the dynamics of a prospective study, the lipid profile of 120 pregnant women with obesity of II and III degrees was studied.

At 8-12 weeks of gestation, the average TC content in obese patients was 5.02 ± 0.032 mmol/l (in the control group – 4.65 ± 0.039 mmol/l, $p < 0.001$), TG level – 1.68 ± 0.016 mmol/l (in the control group – 1.00 ± 0.013 mmol/l, $p < 0.001$). The VLDL content at the same time of gestation was 0.77 ± 0.07 mmol/l (in the control group - 0.46 ± 0.07 mmol/l, $p < 0.01$). LDL levels were 2.69 ± 0.013 mmol/l (in the control group - 2.56 ± 0.020 mmol/l, $p < 0.001$), HDL – 1.86 ± 0.014 mmol/l (in the control group – 1.76 ± 0.022 mmol/l, $p < 0.001$), the value of the atherogenic coefficient is 1.69 ± 0.028 c.u. (in the control group – 1.64 ± 0.077 c.u., $p > 0.05$), HDL/LDL ratio – 0.69 ± 0.07 units (in the control group – 0.68 ± 0.05 units, $p > 0.05$). When comparing lipid metabolism indicators in women of the main and control groups during pregnancy 34-36 weeks, statistically significant differences were also established. The TC, TG, VLDL, and atherogenic coefficient values increase in obesity compared to the control group. Analysis of the lipid profile showed a significant increase in the level of TC in the blood serum of patients of the main group – 6.15 ± 0.050 mmol/l (in the control group - 5.20 ± 0.052 mmol/l, $p < 0.001$), TG - 2.16 ± 0.012 mmol/l (in the control group – 1.42 ± 0.013 mmol/l, $p < 0.001$), VLDL – 0.99 ± 0.05 mmol/l (in the control group – 0.65 ± 0.04 mmol/l, $p < 0.01$). At the same time, the level of LDL in the blood serum of pregnant women of the main group was equal to 3.07 ± 0.017 mmol/l (in the control group – 3.07 ± 0.033 mmol/l, $p > 0.05$), HDL – 1.49 ± 0.09 mmol/l (in the control group – 1.66 ± 0.012 mmol/l, $p < 0.001$), the value

of the atherogenic coefficient – 3.12 ± 0.044 c.u. (in the control group – 2.13 ± 0.038 c.u., $p < 0.01$), HDL/LDL ratio – 0.48 ± 0.06 units (in the control group – 0.54 ± 0.06 units, $p > 0.05$).

To assess the association of the studied clinical and metabolic parameters, a correlation analysis was carried out, which revealed the presence of close relationships between lipid profile parameters and BMI. It was found that the increasing imbalance of lipid profile parameters by 34-36 weeks of pregnancy was accompanied by an increase in body weight: TC ($r = 0.251$; $p = 0.001$), TG ($r = 0.401$; $p = 0.002$), VLDL ($r = 0.365$; $p = 0.033$), HDL ($r = -0.318$; $p = 0.002$).

For the groups of studied pregnant women with obesity, arterial hypertension, and their combination, the TC level was 5.06 ± 0.071 ; 5.05 ± 0.042 and 5.81 ± 0.084 mmol/l, TG – 1.71 ± 0.036 ; 1.68 ± 0.022 and 1.67 ± 0.037 mmol/l, LDL – 2.93 ± 0.037 ; 2.69 ± 0.019 and 2.73 ± 0.030 mmol/l, VLDL – 0.78 ± 0.02 ; 0.77 ± 0.03 and 0.76 ± 0.02 mmol/l, accordingly. In dynamics, by 18-20 weeks of gestation, the increase in TC, TG, LDL, and VLDL in the group of obese pregnant women was 13.8%; 12.8%; 9.3%; 12.7%, in the group of pregnant women with arterial hypertension – 13.0%; 14.8%; 7.0%; 14.2% and in the group of pregnant women with a combination of obesity and arterial hypertension – 19.3%; 14.3%; 4.8%; 14.5%, consequently. The most pronounced dynamics of the lipid spectrum occurred in the group of pregnant women with obesity in combination with arterial hypertension, due to an increase in the level of TC from 4.87 ± 0.071 mmol/l to 5.81 ± 0.084 mmol/l (1.2 times).

Subsequently, by 34-36 weeks of gestation, the increase in TC, TG, LDL, and VLDL in the group of obese pregnant women was 18.8%; 26.3%; 14.5%; and 27.0%, respectively. In the group of pregnant women with arterial hypertension these indicators were 23.3%, 28.5%, 14.8%, and 28.5%, respectively, and with a combination of obesity and arterial hypertension, these indicators were 25.7%, 30.5%, 11.7% and 31.5%.

In obese pregnant women, the state of carbohydrate metabolism was characterized by basal hyperglycemia and hyperinsulinemia. The initial level of glycemia in obese patients was significantly higher than

that of the healthy group by 32.8% ($p < 0.001$). All patients underwent an oral glucose tolerance test (OGT). Statistically significant differences in glycemia during the test were recorded in obese patients at 60 and 120 minutes relative to the control. When performing GTT, an increase in glycemia was detected after a load of 75 g of glucose after 60 minutes – up to 10.34 ± 0.085 mmol/l, which was significantly higher than in the group of healthy individuals (6.11 ± 0.076 mmol/l, $p < 0.001$). At the 120th minute, the glyceimic level decreased (6.47 ± 0.042 mmol/l), but did not reach control values ($p < 0.001$).

The fasting serum insulin level in pregnant women with abdominal obesity was 16.1 ± 0.27 μ IU/ml. At the same time, in obese pregnant women, the fasting insulin level was almost twice as high as in the control group (8.9 ± 0.16 μ IU/ml, $p < 0.001$). The fasting serum glucose level in obese patients was 6.39 ± 0.007 mmol/l and was also higher compared to the control (4.81 ± 0.015 mmol/l, $p < 0.001$).

The insulin resistance index (HOMA-IR) in women with abdominal obesity was 4.57 ± 0.19 units. Moreover, the values of this index were 2.5 times higher than in women in the control group (1.90 ± 0.17 units, $p < 0.001$), which indicates the development of insulin resistance. The glucose-insulin ratio (CARO index), reflecting the degree of compliance with insulin secretion, in the group of obese patients was 27.8% lower than the values in the control group ($p < 0.001$). The CARO coefficient in women with abdominal obesity was slightly higher than the quantitative criterion for insulin resistance (0.33) and was at the level of 0.39 ± 0.09 units. Moreover, the values of the indicator were significantly lower in obese patients than in women in the control group (0.54 ± 0.11 units, $p < 0.001$).

The study of protein metabolism shows that serum albumin levels in the pregnant women of the main group (8-12 weeks) decreased 2.1 times compared to the control group (respectively 2.19 ± 0.008 g/dl and 4.62 ± 0.049 g/dl, $p < 0.001$). When analyzing cytolysis enzymes, it was found that the mean values of ALT and AST at the beginning of pregnancy exceeded the control values and were 32.0 ± 0.20 IU/L and 35.3 ± 0.13 IU/L, respectively (control 12.0 ± 0.09 IU/L and 15.3 ± 0.14 IU/L, $p < 0.001$). At 8-12 weeks of gestation, the

mean values of ALP corresponded to the control values and were 55.9 ± 0.25 units/l (in the control - 45.5 ± 0.14 units/l, $p > 0.05$). The serum urea level was 6.79 ± 0.013 mmol/l, which was significantly different from that in the control group (4.67 ± 0.021 mmol/l, $p < 0.001$). Serum creatinine concentration in obese pregnant women was 1.5 times higher than in the control group (59.7 ± 0.1 μ mol/l vs 92.0 ± 0.21 μ mol/l, $p < 0.001$). The level of microalbuminuria in obese pregnant women ranges from 18.9-38.2 mg/l, on average 25.9 ± 0.41 mg/l, which significantly ($p < 0.001$) exceeds the corresponding indicator in pregnant women of the control group (10.6 ± 0.10 mg/l).

During 34-36 weeks of pregnancy, the dynamics of clinical and laboratory parameters show an increase in serum albumin level (3.59 ± 0.013 g/dl) and a decrease in other parameters. Thus, ALT level is 9.36 ± 0.085 BV/l, AST level - 13.9 ± 0.09 IU/l, ALP level - 37.3 ± 0.16 IU/l), urea level - 3.06 ± 0.007 mmol/l, creatinine level 81.6 ± 0.08 μ mol/l.

ADIPOKINES, METABOLIC PARAMETERS AND MARKERS OF SYSTEMIC INFLAMMATION IN PREGNANT WOMEN

The content of adipokines in serum was examined at 8-12 weeks of gestation. In normal serum, adiponectin varies widely from 23 to 34 μ g/ml. Patients with abdominal obesity had lower levels of adiponectin (mean 21.6 ± 0.65 μ g/ml, $p < 0.05$). The study of serum leptin content in obese pregnant women revealed its increase to 37.9 ± 2.11 ng/ml compared to the control group of pregnant women with normal body weight - 16.5 ± 0.61 ng/ml ($p < 0.001$). Analysis of the study results showed no changes in resistin concentration in obese pregnant women compared to the control group. In the main group, the level of resistin varied from 3.35 to 6.68 ng/ml, the mean value was 4.91 ± 0.198 ng/ml. In the control group, its level fluctuated from 3.43 to 6.62 ng/ml, the mean value was 4.66 ± 0.083 ng/ml. The quantitative evaluation of visfatin level showed a slight decrease in the group of obese pregnant women compared to the group of pregnant

women with normal body weight - 24.0 ± 0.34 ng/ml ($p < 0.05$), indicating the development of hypovisfatinaemia in obese pregnant women.

When analyzing the results of the study in pregnant women with abdominal obesity, a negative correlation was revealed between the level of adiponectin and anthropometric indicators: BMI ($r = -0.364$), WC ($r = -0.397$), TC ($r = -0.251$), WC/TC ($r = -0.249$) ($p < 0.05$). According to our data, the level of leptin in the blood serum in obese pregnant women is closely related to BMI ($r = 0.285$), WC ($r = 0.319$), and TC ($r = 0.380$) ($p < 0.05$). Analysis of the results of the study in pregnant women with abdominal obesity shows a negative correlation between the level of visfatin and anthropometric indicators: BMI ($r = -0.346$), WC ($r = -0.520$), TC ($r = -0.570$), WC/TC ($r = -0.171$) ($p < 0.05$).

A significant inverse relationship was found between the level of adiponectin and insulin ($r = -0.163$, $p < 0.05$) and the HOMA-IR indicator ($r = -0.323$, $p < 0.05$). Correlation analysis of adiponectin level with the studied serum lipid profile parameters showed a positive relationship with TG level ($r = 0.257$; $p = 0.001$). Correlation analysis of leptin level with serum lipid profile parameters showed a positive correlation with LDL ($r = 0.426$, $p < 0.05$) and TG ($r = 0.417$, $p < 0.05$) levels, i.e. lipid level growth is accompanied by adequate leptin growth. There was also a negative correlation between leptin level and HDL ($r = -0.430$, $p < 0.05$). The study revealed a statistically significant direct correlation between leptin and insulin levels ($r = 0.402$, $p < 0.05$) and between leptin levels and HOMA-IR index value ($r = 0.16$, $p < 0.05$). When correlation analysis of visfatin level with the studied serum lipid profile parameters, a negative relationship with LDL ($r = -0.295$), HDL ($r = -0.241$), and TG ($r = -0.219$) levels was obtained ($p < 0.05$). There was a significant inverse relationship between visfatin and insulin levels ($r = -0.132$, $p < 0.05$) and visfatin and HbA1c ($r = -0.121$, $p < 0.05$).

In combined pathology (abdominal obesity+arterial hypertension), mean adiponectinaemia values were significantly lower than control values and were 22.1 ± 0.67 μ g/ml ($p < 0.001$). It should

also be noted the presence of an inverse correlation between adiponectin and the level of SAP ($r = -0.133$) and DAP ($r = -0.167$) in pregnant women with isolated arterial hypertension and a direct correlation between these parameters in pregnant women with isolated obesity (SAP: $r=0.181$; DAP: $r=0.265$) and pregnant women with combined pathology (SAP: $r=0.199$; DAP: $r=0.137$).

In pregnant women with abdominal obesity and type 2 diabetes mellitus, a reduction in blood adiponectin levels was noted compared to the control group. Slightly more pronounced hypoadiponectinemia was detected in obese patients ($21.2 \pm 0.63 \mu\text{g/ml}$, $p < 0.001$). The mean adiponectin level in women with type 2 diabetes mellitus was $25.4 \pm 0.93 \mu\text{g/ml}$ ($p < 0.05$). Leptin level in patients with type 2 diabetes mellitus was $30.4 \pm 1.99 \text{ ng/ml}$, which was higher than control values ($p < 0.001$). Resistin level in pregnant women with type 2 diabetes mellitus was $3.11\text{-}6.29 \text{ ng/ml}$, mean value was $4.35 \pm 0.327 \text{ ng/ml}$.

The concentrations of pro-inflammatory cytokines IL-6 and TNF- α in the blood serum of obese pregnant women were significantly higher than the corresponding values in the control group ($p < 0.001$). At the same time, IL-6 values were 5.2 times higher than control values, and TNF- α values were 8.3 times higher. Compared to the control group, TNF- α significantly increased in all groups of patients. In the group of women with obesity, it was $29.4 \pm 1.10 \text{ pg/ml}$, with arterial hypertension - $30.9 \pm 1.56 \text{ pg/ml}$, with a combination of obesity and arterial hypertension - $27.5 \pm 2.89 \text{ pg/ml}$, with hyperglycemia - $30.5 \pm 1.87 \text{ pg/ml}$ ($p < 0.001$). The highest levels of IL-6 were found in women with hyperglycemia - $6.51 \pm 0.209 \text{ pg/ml}$ and in women with a combination of obesity and arterial hypertension - $6.44 \pm 0.356 \text{ pg/ml}$. In patients with obesity and arterial hypertension, the content of IL-6 in the blood serum was slightly reduced and amounted to $6.07 \pm 0.120 \text{ pg/ml}$ and $6.05 \pm 0.185 \text{ pg/ml}$, respectively ($p < 0.001$).

As the data obtained show, significant associations were also found between the serum concentration of TNF- α and leptin ($r=0.470$, $p=0.054$); TNF- α with visfatin ($r=0.770$, $p=0.049$) IL-6 and leptin ($r=0.424$, $p=0.044$). Correlation analysis showed that an increase in

IL-6 concentration is statistically significantly associated with BMI ($r=0.360$, $p=0.034$).

Obese women showed higher CRP values than the comparison group. This is confirmed by the presence of a positive correlation between the concentration of CRP in the second trimester of pregnancy and BMI ($r=0.243$; $p=0.008$), CRP in the third trimester of pregnancy, and BMI ($r=0.301$; $p=0.001$). There was also a correlation between second-trimester CRP and blood insulin levels ($r=0.788$; $p=0.012$), second-trimester CRP and adiponectin levels ($r=0.458$; $p=0.013$), first-trimester CRP and visfatin levels ($r=0.517$; $p=0.011$). In the third trimester of pregnancy, there was evidence of an association between CRP and leptin values ($r=0.398$, $p=0.033$).

MACROSCOPIC AND PATHOMORPHOLOGICAL CHARACTERISTICS OF CHANGES IN THE PLACENTA AND UMBILICAL CORD OF PREGNANT WOMEN WITH GESTATIONAL AND PERINATAL COMPLICATIONS DURING PREGNANCY

The average size of the placentas obtained from women in the control group is 18x16x2.3 cm and their weight ranges from 500-650 grams. The length of the umbilical cord obtained from women in the control group is within the normal size range of 50-52 cm, diameter 0.8-1.1 cm. Umbilical cord wrapping was not observed in women who had a normal pregnancy. In microscopic examination, no fibrin and inflammatory cells were observed between the chorionic villi. Chorionic clusters are very small - visible under the microscope and are about 30-40 microns in size. The terminal villi of the chorion consist of 1-6 capillaries and are covered with a thin layer of syncytiotrophoblasts. Analysis of the microslides obtained by immunohistochemical staining shows that no positive staining was noted on the images of the basal decidual membrane and chorionic clusters, lacunae, septa, and basal layer included in its mass, which was evaluated as "-". As a result of immunohistochemical staining of

the umbilical cord, no staining was observed in the stroma, the wall of the arterial vessels, or the lumen of the venous vessel.

The average size of placentas obtained from women in the high BMI group is 18.6 x 17.5 x 3.7 cm and their weight ranges from 656 to 712 grams. The umbilical cord is located at the periphery of the placenta, its length was 54-56 cm, diameter - 0.9-1.3 cm.. CD3 immunohistochemical staining at microscopic examination revealed focal positive staining on images obtained by staining the basal decidual membrane of the placenta as well as the chorionic clusters, lacunae, septa, and basal layer included in the mass of preparations made from placental tissue obtained from pregnant women with high BMI compared to the control group. Thus, 1 (weak) positive “+” staining was observed in the stroma located between the chorionic villi. Immunohistochemical staining was not observed along the tissue structures constituting the umbilical cord wall and in the wall of arteries, in the basal membranes of vessels, as well as in endothelial cells.

Placentas obtained from women with insulin resistance and type 2 diabetes mellitus had an average size of 18.3 x 16.5 x 3.6 cm, and weight ranged from 700 to 711 grams. In the placentas of women in this group, the umbilical cord is located in equal proportions, being central and peripheral. The blood vessels located in the layer of the placental membrane are stretched, but there are no visible signs of dystrophic calcinosis. On macroscopic examination, the length of the umbilical cord in pregnant women with insulin resistance and type 2 diabetes mellitus was 60-62 cm, and its diameter was 1.1-1.5 cm. Diffuse positive staining on images obtained by staining of basal decidual membrane and chorionic villi, lacunae, septa, and basal lamina in preparations prepared from placental tissue of women with insulin resistance and type 2 diabetes mellitus compared to controls with immunohistochemical CD3 staining: 1 positive "+" 15%, 2 positive "++" 5% and 3 positive "+++" 1% and unstained cells 79%.

The average size of placentas obtained from women in the arterial hypertension group was 17.9x16.5x3.8 cm, and their weight ranged from 598-698 grams. In the placentas of women in this group,

the umbilical cord was located more peripherally. On macroscopic examination of the placentas of pregnant women with arterial hypertension, the length of the umbilical cord was 60-64 cm, its diameter was 0.8-1.5 cm.. Immunohistochemical CD3 staining on images obtained by staining of basal decidua and chorionic villi, lacunae, septa, and basal layer in the placenta and umbilical cord tissue preparations of women in the arterial hypertension group diffuse 1 positive "+" 2%, 2 positive "++" 1% and 3 positive "+++" 1% and unstained cells were 96%.

In pregnant women with high BMI and arterial hypertension, the average size of their placentas was 19.1x17.5x3.8 cm, and their weight ranged from 703-800 grams. The umbilical cord is located both in the center and on the periphery, its length was 62-66 cm, and its diameter was 1.1-1.7 cm. At microscopic examination with immunohistochemical stain CD3, diffuse positive staining was observed on images obtained by staining of the basal decidual membrane and chorionic villi, lacunae, septa, and basal layer of preparations made from placenta tissues obtained from pregnant women with high body mass index and arterial hypertension. Diffuse positive "+" (20%) staining was observed in the stroma, decidua basalis, and amnion cells located between the chorionic villi.

PROGNOSTIC VALUE OF CLINICAL AND METABOLIC DISORDERS DURING PREGNANCY

The next stage of our study was an analysis of the predictive significance of clinical and laboratory markers in pregnant women with obesity, arterial hypertension and hyperglycemia. A comparative analysis of risk factors in the development of obesity and concomitant pathologies made it possible to identify clinical, anamnestic and social signs that have a certain prognostic significance.

For the primary identification of risk factors for the development of metabolic complications in pregnant women, it is necessary, first of all, to use signs with high sensitivity values - more than 50%. High sensitivity values of the studied signs indicate that the results of the

study will be positive in the development of metabolic disorders in pregnant women.

Thus, the clinical and anamnestic signs with high sensitivity in the group of pregnant women with obesity include hereditary aggravation of obesity (84%), eating disorders (95%), and low physical activity (91%). The clinical and anamnestic signs with high sensitivity in the group of pregnant women with arterial hypertension include hereditary aggravation of arterial hypertension (88%). The clinical and anamnestic features with high sensitivity in the group of pregnant women with arterial hypertension and obesity include hereditary aggravation for arterial hypertension (76%) and hereditary aggravation for obesity (77%). Clinical and anamnestic features with high sensitivity in the group of pregnant women with hyperglycemia include hereditary aggravation of diabetes mellitus (64%) and concomitant type 1 diabetes mellitus (82%).

To study the relationships between clinical and anthropometric data, parameters of carbohydrate and lipid metabolism, adipocytokines and markers of systemic inflammation, we performed a correlation analysis of the results obtained. As a result of the analysis, various intersystemic and intrasystemic correlations were established.

The association of hormonal and metabolic parameters studied in the first trimester of pregnancy showed a close correlation between adipocytokine levels, markers of systemic inflammation, insulin resistance, dyslipidemia, and anthropometric data.

Taking into account the data obtained, the work carried out a comparative analysis of metabolic disorders in pregnant women depending on the presence or absence of risk factors. Considering that the probability of metabolic disorders is determined not by one but by many factors, we selected the variables to be included in the prediction model to identify the combination of predictors with the greatest prognostic significance. Using correlation analysis, the most significant predictors were identified and included in the model for predicting metabolic disorders in pregnant women in the early period of gestation.

The mathematical analysis of risk factors allowed us to identify the most significant risk factors, which allowed us to develop a model for predicting the development of metabolic complications in early pregnancy. Taking into account clinical-anamnestic, anthropometric, and laboratory risk factors, the model for predicting metabolic complications in early pregnancy has the following form (Figure 2).

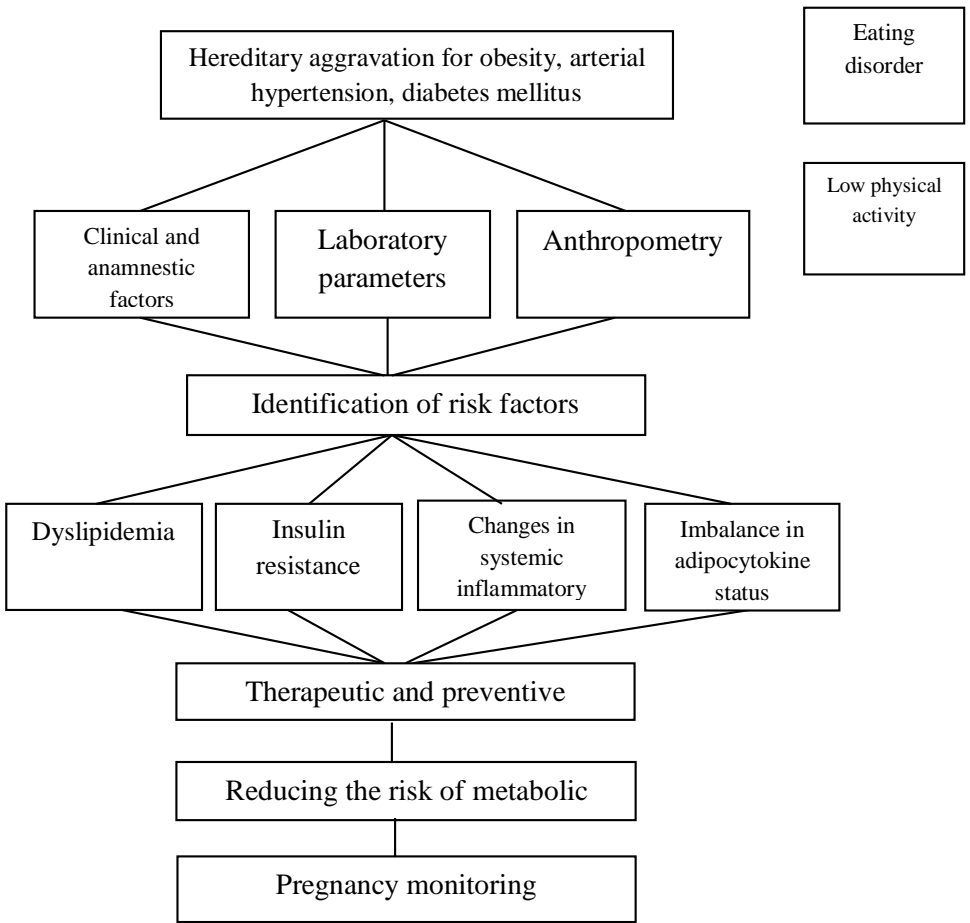


Figure 2. Model for predicting the development of metabolic disorders in early pregnancy

Assessing the eating behavior and anthropometric parameters of women during the pre-pregnancy period is crucial. Understanding the pathophysiology of metabolic disorders and identifying women at risk are key aspects of effective prevention of metabolic complications during pregnancy.

Based on the results obtained, we established prognostic clinical-anthropometric and laboratory risk factors in the development of metabolic syndrome in pregnant women in early gestation. The results of our comprehensive clinical and laboratory study allowed us to develop a model of measures based on the possibility of managing risk factors for metabolic complications in pregnancy. The developed model is based on the analysis of clinical and anamnestic predictors, monitoring of biochemical indicators of metabolism, cytokine status, and assessment of adipocytokine balance.

THE COURSE OF PREGNANCY, CHILDBIRTH AND THE CONDITION OF NEWBORNS IN OBESE MOTHERS

In the first trimester, pregnancy without complications was observed in the control group more often than in groups of pregnant women with obesity and metabolic disorders (60.0%, $p < 0.05$). One of the most common complications of the first trimester is the pathological conditions of the first half of pregnancy (control group 21.2%, obesity 34.5%, arterial hypertension 44.0% ($p < 0.05$), obesity and arterial hypertension 21.7%, type 2 DM 33.3%). Threatened early miscarriage was the most frequent complication of the first trimester of pregnancy in the group of pregnant women with obesity and arterial hypertension - 52.1% ($p < 0.05$). Its frequency was 31.0% in obese pregnant women, 38.9% in patients with arterial hypertension, 22.2% in women with type 2 diabetes mellitus, and 12.5% in pregnant women in the control group. Activation of intravascular thrombogenesis complicated the first trimester of pregnancy in 3.4% of obese patients, in 3.4% of patients with arterial hypertension, in 4.3% of patients with obesity and arterial hypertension, and 22.2% of patients with type 2 diabetes mellitus.

Analysis of the features of the course of the II trimester shows that pregnancy is uncomplicated in an approximately equal number of cases in all groups (obesity - 44.8%, arterial hypertension - 44.0%, obesity and arterial hypertension - 43.4%, type 2 diabetes mellitus - 33.3%). The most common complication of the second trimester was threatened miscarriage. The incidence of this complication was 23.7% in the control group, 34.4% in the obese pregnant group, 42.3% ($p < 0.05$) in arterial hypertension, 17.3% in obesity and arterial hypertension, and 44.4% in type 2 diabetes mellitus.

In the third trimester, the rate of uncomplicated pregnancy was 43.7% in the control group, 13.8% in the obesity group, 15.2% in the arterial hypertension group, 13.0% in the obesity and arterial hypertension group, and 11.1% in the type 2 diabetes mellitus group ($p < 0.05$). There were no significant differences in the frequency of threatened preterm birth in the third trimester of pregnancy: in the control group - 2.5%, in the obesity group - 3.4%, in the arterial hypertension group - 1.7%, in the obesity and arterial hypertension group - 4.3%, in the group of type 2 diabetes mellitus - 11.1% ($p > 0.05$) (Table 1).

The frequency of natural childbirth was the highest in the control group, i.e. 76.3% among pregnant women with baseline normal body weight and without any metabolic disorders. Among the patients in the main group, the frequency of natural childbirth in pregnant women with obesity and arterial hypertension (17.4%, $p < 0.05$) and in pregnant women with arterial hypertension (40.7%, $p < 0.05$) was statistically less reliable than in the control group. In 58.6% of obese patients and 44.4% of type 2 Diabetes mellitus patients, childbirth ended naturally. The frequency of cesarean delivery in the control group was 23.7%.

In the main group, it was higher in patients with arterial hypertension (59.3%) and among patients with arterial hypertension on the background of obesity (82.6%) ($p < 0.05$).

Table 1.

Complications in the third trimester of pregnancy

Pregnancy complications	Observation groups				
	Control group (n=80)	Obesity (n=29)	Arterial hypertension (n=59)	Obesity + arterial hypertension (n=23)	Type 2 Diabetes mellitus (n=9)
Uncomplicated course	35/43,7%	4/13,8%*	9/15,2%*	3/13,0%*	1/11,1%*
Risk of premature childbirth	2/2,5%	1/3,4%	1/1,7%	1/4,3%	1/11,1%
Hereditary thrombophilias	21/26,2%	6/20,7%	8/13,6%	3/13,0%	1/11,1%
Anaemia of pregnancy	15/18,7%	4/13,8%	10/16,9%	2/8,7%	1/11,1%
Moderate preeclampsia	3/3,7%	4/13,8%	15/25,4%*	7/30,4%*	4/44,4%*
Fetal growth restriction syndrome	-	1/3,4%	5/8,4%*	2/8,7%	1/11,1%
Hypercoagulability syndrome	-	1/3,4%	2/3,4%	2/8,7%	-
Polyhydramnios	3/3,7%	2/6,9%	5/8,4%	1/4,3%	-
Chronic fetal hypoxia	1/1,2%	6/20,7%*	4/6,8%	2/8,7%	-

Note: p<0.05 compared to the control group.

The highest frequency of large fetus childbirth was observed in obese women – 10 (34.4%) and in the group with obesity and arterial hypertension – 6 (26.0%) ($p<0.05$). Various complications of the early neonatal period were recorded in 31 (38.8%) newborns in the control group and 65 (54.1%) in the main group ($p<0.05$). Various

complications of the early postpartum period were noted in 25 (31.3%) patients in the control group and 49 (40.8%) patients in the main group.

The present study analyzed the relationship between maternal obesity factor and neonatal birth weight, which showed that obesity increases the risk of macrosomia by 2.72 times (OR=2.72; CI=1.95-3.78). Analysis of the relationship between maternal metabolic syndrome factors and neonatal weight showed a higher relative risk (OR=5.33; CI=1.66-17.12). It was found that the risk of developing moderate preeclampsia in the second half of pregnancy in women with obesity and metabolic disorders is 6.67 times higher than with normal body weight (OR=6.67; CI=2.10-21.10). In a comparative analysis of metabolic disorders with chronic fetal hypoxia, the risk of developing it was found to be 8.0 times higher than in the control group (OR=8.00; CI=1.06-60.32).

Basic principles of a pregnancy planning program for obese women:

Stage 1 of the program

- Initial detection of obesity and overweight in women of reproductive age during pregnancy planning.
- If obesity or overweight is detected, it is necessary to specify the degree of disturbance of carbohydrate and lipid metabolism and the presence of hypertensive complications.
- Specialist consultation.

The first stage of the program is important to provide a comprehensive and complete examination for the development of further tactics for planning and preparation for pregnancy in women with obesity and metabolic disorders (Table 2).

Based on the results of the complex clinical and laboratory examination, the 2nd stage of the pregnancy planning program should be started.

Stage 2 of the program

- women diagnosed with obesity need to undergo weight correction.
- *The main ways of weight correction:*

- *Psychological correction.* An important principle of treatment is its personalization, taking into account the psycho-emotional status of the woman. It is recommended to buy the manifestations of eating disorders to create personal motivation for long-term treatment and abandonment of bad habits (consultation with a medical psychologist is necessary).

Table 2.

Diagnostic measures

Diagnostic methods	Clinical diagnostic studies
Clinical-anamnestic	Collection of anamnesis: complaints, aggravated heredity, psychological factors, nutritional status, physical activity, use of alcohol, narcotic drugs, antidepressants, smoking, blood pressure level and previous hypotensive therapy, dyslipidemia level and previous correction, glycemia level and previous correction, concomitant somatic diseases, gynecological and obstetric history
Anthropometric	Measurement of waist circumference (WC), thigh circumference (TC), calculation of WC/TC index, calculation of body mass index (BMI)
Fat metabolism study	Total cholesterol, triglycerides, high-density lipoproteins, low-density lipoproteins
Carbohydrate metabolism study	Insulin content, assessment of insulin resistance (HOMA-Ir index, Caro index), oral glucose tolerance test
Adipocytokines status study	Leptin, adiponectin, visfatin, resistin
Specialist consultation	Therapist, endocrinologist, cardiologist, obstetrician -gynecologist

- *Diet therapy.* A balanced diet with proper calorie distribution is recommended (consultation with a dietician is required).

- *Physical activity.* Dosed physical activity is recommended, taking into account the somatic status of patients (under the supervision of a doctor of physical therapy).
- *Pharmacotherapy* (consultation with an endocrinologist is necessary, and a cardiologist is required if indicated).
- The second stage of the pregnancy planning program is considered effective when:
- reduction of body weight, reduction of WC, TC, WC/TC and BMI
- normalization of the level of total cholesterol, triglycerides, HDL and LDL, normalization of fasting blood glucose levels, normalization of blood pressure.

The duration of the second stage of the pregnancy planning program is 3-6 months. After the planned pregnancy, it is necessary to further adjust the management of patients by an obstetrician-gynecologist, therapist, endocrinologist, and cardiologist.

RESULTS

1. The conducted study allowed us to present the clinical-anamnestic and medical-social characteristics of 550 pregnant women, among whom 213 (45.3%) patients were diagnosed with increased BMI and obesity [1,2,5,6].
2. The medical and social characteristics of obese pregnant women include 29.8 ± 0.54 years old; hereditary complications (84.0%); high WC (90.0 ± 0.73 cm), TC (99.1 ± 0.72 cm), BMI (39.5 ± 0.57 kg/m²), WC/TC (0.90 ± 0.004 VA), high WHtR (0.56 ± 0.003 VA); mixed eating disorder (51.6%); low physical activity (91.0%); secondary education (58.4%); predominantly urban dwellers (66.2%); prevalence of cardiovascular disease history (40.38%, $p < 0.001$). These are pathogenetic factors in the development of gestational complications [3,6,9,11,12].
3. In lipid metabolism in obese pregnant women, significantly higher levels of TC, TG, and VLDL in the blood serum should be noted already in the first trimester of pregnancy and a further increase with increasing gestational age, as well as a decrease in the level of HDL ($p < 0.001$). The development of pregnancy is accompanied by an increase in lipid metabolism at 18-20 and 34-36 weeks of gestation, respectively: TC - by 14.3% and 22.5%, LDL - by 7.4% and 14.1%, TG - by 14, 2% and 28.5%, VLDL - by 14.2% and 28.6%, a decrease in HDL - by 5.4% and 19.8%, which leads to an increase in the atherogenic coefficient by 33.7% and 84.6 %, respectively, and is a risk factor for the transformation of physiological dyslipidemia into pathological. Obese pregnant women are characterized by changes in carbohydrate metabolism with a higher frequency of hyperglycemic states with a gradual increase in insulin resistance. The values of the HOMA-IR index in obese pregnant women are 2.5 times higher, the CARO index is 27.8% lower than the values in the control group ($p < 0.001$), and the HbA1c level is 8.6%, which is higher than the control values ($p < 0.001$) [13,16,19,21].

4. Obese pregnant women are characterized by hypoadiponec-tinemia (21.6 ± 0.65 $\mu\text{g/ml}$, $p < 0.05$), hypovisfatinemia (24.0 ± 0.34 ng/ml , $p < 0.05$), and hyperleptinemia (37.9 ± 2.11 ng/ml , $p < 0.001$). A negative correlation was obtained ($p < 0.05$) between the level of adiponectin and WC ($r = -0.397$), TC ($r = -0.251$), WC/TC ($r = -0.249$) and BMI ($r = -0.364$), which indicates an inverse relationship between the level of adiponectin and total body fat (BMI) and the nature of its distribution (WC). Leptin level is closely related to BMI ($r = 0.285$), WC ($r = 0.319$), and TC ($r = 0.380$) ($p < 0.05$) and indicates the development of leptin resistance. Negative correlation between the level of visfatin and anthropometric indicators: BMI ($r = -0.346$), WC ($r = -0.520$), TC ($r = -0.570$), WC/TC ($r = -0.171$) ($p < 0.05$) indicates a decrease in its level with an increase in adipose tissue mass [13,16,19,21].
5. Views on the mechanisms of obesity have been expanded. A significant inverse relationship was revealed between the level of adiponectin and insulin ($r = -0.163$, $p < 0.05$), the HOMA-IR indicator ($r = -0.323$, $p < 0.05$), HDL ($r = -0.318$), and a positive relationship with TG ($r = 0.257$; $p = 0.001$), which characterizes hypoadiponec-tinemia as a link between obesity, insulin resistance and atherogenic changes in blood serum. A statistically significant direct correlation was established between the level of leptin and insulin ($r = 0.402$, $p < 0.05$) and the value of the HOMA-IR index ($r = 0.16$, $p < 0.05$), which indicates the participation of leptin in the mechanisms of development of insulin resistance.
Metabolic risk factors such as abdominal obesity, carbohydrate metabolism disorders, and dyslipidemia are directly involved in the development and maintenance of inflammation, which is manifested by an increase in the level of pro-inflammatory cytokines IL-6 - 5.2 times, TNF- α - 8.3 times ($p < 0.001$) and the level of CRP – up to 8.24 ± 0.18 mg/l ($p < 0.05$). The presence of a significant direct relationship between the level of TNF- α and leptin ($r = 0.470$, $p = 0.054$), IL-6 and leptin ($r = 0.424$, $p = 0.044$),

CRP and leptin ($r=0.398$, $p=0.033$) indicates the formation of a pro-inflammatory state on the background of increased leptin levels and the progression of obesity [19,21].

6. Pathomorphological changes in the placentas of women with obesity and concomitant metabolic disorders are characterized by different structural and functional organization (decrease in the volumetric density of chorionic villi, the number and numerical density of capillaries in the terminal villi, narrowing of the intervillous space, changes in the lumen of the sinusoidal capillaries of the terminal villi), which determines the degree of its severity compensatory possibilities [20].
7. Women with a combination of abdominal obesity, dyslipidemia, diabetes mellitus, and arterial hypertension represent a high-risk group for the development of complications of pregnancy, which requires in-depth examination aimed at detecting early signs of gestational complications. In the first trimester, the highest frequency of early toxicosis was characteristic of pregnant women with arterial hypertension (44.0%), and threatened miscarriage - for pregnant women with obesity and arterial hypertension (52.1%). In the second trimester, threatened abortion was more frequent in the group with arterial hypertension (42.3%) and the hypercoagulable syndrome was more frequent in the group with type 2 diabetes mellitus (22.2%). In the third trimester, moderate preeclampsia was more frequent in the groups with arterial hypertension (25.4%), obesity and arterial hypertension (30.4%), type 2 diabetes mellitus (44.4%); fetal retardation syndrome - in the group with arterial hypertension (8.4%); chronic fetal hypoxia - in pregnant women with obesity (20.7%) [4,7,8,18].
8. Analysis of the relationship between maternal obesity and the newborn's body weight showed that obesity increases the risk of macrosomia by 2.72 times ($OR=2.72$; $CI=1.95-3.78$; $\chi^2=20.535$; Cramer's criterion $=0.394$; $p < 0.001$). The risk of developing moderate preeclampsia in the second half of pregnancy in women with obesity and metabolic disorders is 6.67 times higher

than with normal body weight (OR=6.67; CI=2.10-21.10; $\chi^2=15.482$; Cramer's criterion = 0.279; $p<0.001$) [22].

9. The postpartum period proceeded without complications in 55 (68.7%) women of the control group, 17 (58.6%) patients of the group with obesity ($p>0.05$), 42 (71.1%) women of the group with arterial hypertension ($p>0.05$), in 9 (39.1%) patients of the group with obesity and arterial hypertension ($p<0.05$) and 3 (33.3%) women of the group with type 2 diabetes mellitus ($p<0.05$). In 25 (31.3%) women of the control group and in 49 (40.8%) patients of the main group, various complications of the course of the early postpartum period were noted. Various complications of the early neonatal period were noted in 31 (38.8%) newborns from the control group and in 65 (54.1%) newborns from the main group ($p<0.05$) [14].
10. Dispensary monitoring of obese pregnant women should be personalized due to the high risk of perinatal and obstetric complications. A model for predicting the development of metabolic complications in early pregnancy based on a mathematical and statistical analysis of clinical and anamnestic predictors, comprehensive assessment of insulin resistance, dyslipidemia, leptin resistance, adipocytokine status, and inflammatory markers was developed [10,22].

PRACTICAL RECOMMENDATIONS

1. The high prevalence, clinical and medical-social significance of obesity in women necessitate the identification of risk factors and metabolic disorders in early pregnancy using the proposed prediction model, which will make it possible to implement timely diagnostic and therapeutic and preventive measures.
2. Implementation of the basic principles of the proposed two-stage program of measures during pregnancy planning in obese women will help to avoid the risk of gestational complications in the future.
3. It is necessary to recommend that all obese women planning to conceive should be included in a dispensary group for comprehensive training aimed at weight loss and normalization of lipid and carbohydrate metabolism.
4. In pregnant women with obesity and risk of metabolic disorders, along with routine assessment of lipid and carbohydrate metabolism, it is recommended to determine the indicators of hormonal-adipokine regulation. For this purpose, the examination plan should include the determination of adiponectin, leptin, and visfatin levels.

List of published scientific papers on the subject of the dissertation

1. Тагиева Ф.А. Ожирение и репродуктивное здоровье женщины. // Актуальні проблеми сучасної медицини: Вісник Української медичної стоматологічної академії. Ukraina, 2016. Т. 16. № 2 (54). с. 317-320.
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List of abbreviations

AI	– atherogenic index
ALP	– alkaline phosphatase
ALT	– alanine aminotransferase
AR	– absolute risk
AST	– aspartate aminotransferase
AT	– arterial pressure
BMI	– body mass index
CDRF	– chance of detecting a risk factor
CI	– confidence interval
CRP	– C-reactive protein
DAP	– diastolic arterial pressure
DET	– diagnostic efficiency or accuracy of the test
DM	– diabetes mellitus
ELISA	– Enzyme-Linked Immunosorbent Assay
FN	– false negative
FP	– false positive
GDM	– gestational diabetes mellitus
GTT	– glucose tolerance test
HbA1c	– glycated hemoglobin
HDL	– high-density lipoproteins
HOMA-IR	– Homeostasis Model Assessment-
ICD	– International Classification of Diseases
IHC	– Immunohistochemical
IL-6	– interleykin-6
IR	– insulin resistance
IU	– international unit
LDL	– low-density lipoproteins
LH	– luteinizing hormone
LR	– leptin resistance
NPV	– negative prognostic value
NRR	– negative reliability ratio
OGT	– oral glucose tolerance test
OR	– Odds ratio

POS	– polycystic ovary syndrome
PPV	– positive prognostic value
PRR	– positive reliability ratio
PSI	– Predictive Summary Index
RD	– risk difference
RR	– relative risk
RRI	– relative risk index
RRR	– relative risk reduction
S	– sensitivity
SAP	– systolic arterial pressure
Sp	– specificity
TC	– thigh circumference
TC	– total cholesterol
TG	– triglyceride
TN	– true negative
TNF-α	– tumor necrotic factor- α
TNR	– true negative ratio
TP	– true positive
TPR	– true positive ratio
VLDL	– very-low-density lipoproteins
WC	– waist circumference
WHtR	– waist-height ratio
WHU	– World Health Organization
Yi	– Yudin index

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